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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,417	11/24/2003	Kun-Liang Guan	UM-08469	5108

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EXAMINER

WOOD, AMANDA P

ART UNIT	PAPER NUMBER
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1657

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/720,417

Applicant(s)

GUAN, KUN-LIANG

Examiner

Amanda P. Wood

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 34-50 is/are pending in the application.
- 4a) Of the above claim(s) 36-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34-35, 45-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election of the species "type 2 diabetes" as the species of disease, "mTOR" as the defective element, and "rapamycin" as the agent administered, in the reply filed on 14 August 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 36-44 have been withdrawn as being drawn to non-elected species.

Claims 34, 35, 45-50 are presented for consideration on the merits.

Claim Objections

Claim 48 is objected to because of the following informalities: The phrase "complications associated with" appears to be repeated once in error in line 2. Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

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F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 34-35 and 45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10, 17, and 18 of copending Application No. 10/639,263. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to methods of treating a disease comprising administering an agent that reduces cellular ATP levels to a subject suffering from a disease comprising defective cells, wherein the agent is rapamycin and the defective cells are caused by a defective element in mTOR.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34, 35, 45-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

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which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 34 (in lines 4 and 7) and 45 (in line 1) contain the phrase "defective cellular energy status." There is insufficient support for the phrase "defective cellular energy status" in the instant specification. Accordingly, this phrase is deemed new matter.

Claims 46 (lines 1-2) and 50 (lines 1-2) contain the phrase "said disease is complications associated with type 1 diabetes mellitus." In addition, Claim 49 contains the phrase "renal dysfunction" in line 2. There is insufficient support for the disease "type 1 diabetes mellitus" in the instant specification, and in addition, there is insufficient support for a disease comprising "complications associated with type 1 diabetes mellitus" in the instant specification." Furthermore, there is insufficient support for complications comprising "renal dysfunction." Accordingly, these phrases are deemed new matter.

Claims 47 (lines 1-2) and 49 (lines 1-2) contain the phrase "said disease is complications associated with type 2 diabetes mellitus." In addition, Claim 49 contains the phrase "renal dysfunction" in line 2. There is insufficient support for the disease "type 2 diabetes mellitus" in the instant specification, and in addition, there is insufficient support for a disease comprising "complications associated with type 2 diabetes mellitus" in the instant specification." Furthermore, there is insufficient support for complications comprising "renal dysfunction." Accordingly, these phrases are deemed new matter.

Claim 48 (lines 1-2) contains the phrase "said disease is complications associated with complications associated with metabolic syndrome." There is insufficient support for a disease comprising "metabolic syndrome" and further for complications associated with a disease comprising "metabolic syndrome." Accordingly, this phrase is deemed new matter.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, first paragraph for the reasons set forth above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 46 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, it is unclear what Applicant means by the phrases "wherein said disease is complications associated with type 1 diabetes mellitus" and "wherein said complications associated with type 1 diabetes mellitus comprise renal dysfunction" in claims 46 and 50, respectively, (i.e., it is unclear whether the disease from which the subject suffers is type 1 diabetes mellitus or whether Applicant considers the disease to be the complications, e.g., renal dysfunction, associated with the diabetes to be the disease). For purposes of examination, the Examiner will assume that Applicant considers the disease to be type 1 diabetes mellitus.

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Claims 47 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, it is unclear what Applicant means by the phrases "wherein said disease is complications associated with type 2 diabetes mellitus" and "wherein said complications associated with type 2 diabetes mellitus comprise renal dysfunction" in claims 47 and 49, respectively, (i.e., it is unclear whether the disease from which the subject suffers is type 2 diabetes mellitus or whether Applicant considers the disease to be the complications, e.g., renal dysfunction, associated with the diabetes to be the disease). For purposes of examination, the Examiner will assume that Applicant considers the disease to be type 2 diabetes mellitus, particularly since Applicant specified in the species election that the disease chosen to be searched was "type 2 diabetes mellitus."

Claim 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, it is unclear what Applicant means by the phrase "said disease is complications associated complications with associated with metabolic syndrome" in lines 1-2 (i.e., it is unclear whether Applicant considers the disease to be metabolic syndrome, or the complications associated with metabolic syndrome, and further, it is unclear what complications Applicant wishes to claim, based upon the lack of guidance provided in the specification with respect to complications associated with metabolic syndrome). For purposes of examination, the Examiner will assume that Applicant considers the disease to be metabolic syndrome.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 34, 35, and 45 are rejected under 35 U.S.C. 102(a) as being anticipated by Dennis et al (Science 2001).

Dennis et al teach that the mTOR pathway is influenced by the intracellular concentration of ATP and that ATP itself is an ATP sensor. Dennis et al teach that phase 1 clinical trials have shown the importance of understanding the molecular mechanisms that control mTOR function by demonstrating that rapamycin is efficacious in the treatment of solid tumors in patients with metastatic renal cell carcinoma and non-small cell lung, prostate, and breast cancer (i.e., administration of an agent to subjects suffering from a disease comprising cells with a defective cellular energy status, wherein the agent reduces cellular ATP levels). Furthermore, Dennis et al beneficially teach that intracellular concentrations of ATP directly regulate mTOR, and that if tumors gain an mTOR-specific growth advantage because of increased production of ATP, they may be more susceptible to the effects of rapamycin (see, for example, Abstract, pg. 1102, and pg. 1104).

Therefore, the reference is deemed to anticipate the instant claims above.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 34, 35, 46, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Baeder et al (US 5,321,009).

A method of treating a disease comprising providing a subject suffering from a disease and an agent that reduces cellular ATP levels and administering said agent to said subject, wherein said disease is type 1 diabetes mellitus, is claimed.

Baeder et al teach a method of administering rapamycin to patients to prevent the onset or development and to arrest the progression of type 1 diabetes mellitus (i.e., a method of treating a subject suffering from a disease comprising cells having a defective energy status, wherein an agent is administered that reduces cellular ATP levels). Baeder et al teach that renal failure is one of many complications associated with type 1 diabetes mellitus that commonly occurs even with exogenously supplied insulin treatment. Baeder et al teach that an autoimmune response mediated by T-cells occurs initially in type 1 diabetes mellitus that destroys the β -islet cells which produce insulin. Baeder et al further teach that rapamycin has been shown to inhibit murine T-cell activation, and that rapamycin is useful in arresting the development or retarding the progression of type 1 diabetes mellitus (i.e., wherein rapamycin is administered to patients suffering from diabetes). Furthermore, Baeder et al teach that the classic symptoms of type 1 diabetes mellitus only appear once 80% of β -islet cells have been

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destroyed, but that patients suffering from the disease can be detected before they reach that state by detecting associated autoantibodies and other selective markers, in addition to diminished glucose tolerance, which can be observed in patients decades before development of type 1 diabetes. Therefore, Baeder et al teach that patients can suffer from type 1 diabetes long before they reach the point at which enough β -islet cells have been destroyed that they see classic symptoms, and therefore, Baeder et al teach a method wherein rapamycin is administered to these patients who suffer from type 1 diabetes to prevent the progression of the disease (see, for example, Abstract, col. 1, lines 10-60, col. 2, lines 35-67, col. 7, lines 20-65, and col. 8, lines 5-60).

Therefore, the reference is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 34, 35, 46, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baeder et al (US 5,321,009).

A method of treating a disease comprising providing a subject suffering from a disease and an agent that reduces cellular ATP levels and administering said agent to said subject, wherein said disease is type 1 diabetes mellitus, is claimed.

Baeder et al beneficially teach a method of administering rapamycin to patients to prevent the onset or development and to arrest the progression of type 1 diabetes mellitus (i.e., a method of treating a subject suffering from a disease, wherein said disease is type 1 diabetes mellitus, and wherein an agent is administered that reduces cellular ATP levels). Baeder et al teach that renal failure (i.e., an end-result of renal dysfunction) is one of many complications associated with type 1 diabetes mellitus that commonly occurs even with exogenously supplied insulin treatment (i.e., renal failure commonly occurs in diabetes patients on regular treatment), and therefore, Baeder et al beneficially teach a method wherein rapamycin is administered to subjects who likely are experiencing or will experience complications associated with type 1 diabetes, e.g., renal dysfunction. Baeder et al further teach that an autoimmune response mediated by T-cells occurs initially in type 1 diabetes mellitus that destroys the β -islet cells which produce insulin. Baeder et al further teach that rapamycin has been shown to inhibit murine T-cell activation, and that rapamycin is useful in arresting the development or retarding the progression of type 1 diabetes mellitus (i.e., wherein rapamycin is administered to patients suffering from diabetes. Furthermore, Baeder et al teach that the classic symptoms of type 1 diabetes mellitus only appear once 80% of β -islet cells have been destroyed, but that patients suffering from the disease can be detected before they reach that state by detecting associated autoantibodies and other selective

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markers, in addition to diminished glucose tolerance, which can be observed in patients decades before development of type 1 diabetes. Therefore, Baeder et al beneficially teach that patients can suffer from type 1 diabetes long before they reach the point at which enough β -islet cells have been destroyed that they see classic symptoms, and therefore, Baeder et al teach a method wherein rapamycin is administered to these patients who suffer from type 1 diabetes to prevent the progression of the disease (see, for example, Abstract, col. 1, lines 10-60, col. 2, lines 35-67, col. 7, lines 20-65, and col. 8, lines 5-60).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to treat a subject suffering from a disease such as diabetes type 1 based upon the beneficial teachings provided by Baeder et al, with respect to the art-recognized method of administering rapamycin to such patients as a means of preventing the progression of β -islet cell destruction, as discussed above.

Furthermore, Baeder et al particularly point out that the destruction of β -islet cells in type 1 diabetes mellitus starts occurring long before actual clinical symptoms are seen in patients, and that patients can be suffering from the disease (i.e., the destruction of β -islet cells) before the appearance of symptoms, and therefore it would be beneficial to treat patients with rapamycin to prevent the onset of the actual classic symptoms.

Furthermore, it would have been both obvious and beneficial for the skilled artisan to use the methods taught by Baeder et al so as to treat patients suffering from a disease such as diabetes type 1 or complications associated therewith, such as renal dysfunction based upon the teachings that patients suffering from diabetes type 1

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commonly suffer from renal failure (i.e., an end-result of renal dysfunction), for the expected benefit of alleviating both diabetic symptoms and preventing development of the complications associated with diabetes type 1.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda P. Wood whose telephone number is (571) 272-8141. The examiner can normally be reached on M-F 8:30AM -5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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CHRISTOPHER R. TATE
PRIMARY EXAMINER